REMARKS

The Office Action mailed December 16, 2010, was reviewed and the comments of the Patent and Trademark Office were considered.

As of the last amendment, claims 1-3, 5, 7-10 and 12-42 are pending and 1, 2, 8, 16 and 27-34 were withdrawn from consideration. By this response, claims 3, 7, 9, 10, 12-15, 17-19, 21 and 35-37 are amended and claims 14, 21, 24, 41 and 42 are cancelled. No new matter has been added by this Amendment. Support for the amendment can be found generally in the original claims and specification.

Rejection of claims under 35 U.S.C. § 103

The Examiner rejects claims 3, 5, 7, 9, 10, 12-15, 17-26, and 35-42 under 35 U.S.C. § 103(a) as allegedly being unpatentable over WO00/30618 ("Huille"), U.S. Patent No. 7,030,155 ("Lambert") and U.S. Patent No. 5,102,872 ("Singh") as evidenced by the Handbook of Chemistry and Physics, 88th Ed. 2008 and Akiyoshi et al. (J. Controlled Release, 1998; 54:313-320).

The Examiner argues that Huille teaches the concentration of the polymers between 15 and 50 mg/ml, which is the concentration claimed in claim 19 which is dependent on claims 7 and 3. First Applicants would like to correct the dependency of this claim which was erroneously entered by preliminary amendments. In fact claim 19 depends on claims 17 or 18, wherein said polymer has an hydrophobic group derived from tocopherol or cholesterol, $1\% \leq [n/(n+m)] \times 100 \leq 10\%$, and $n + m$ varies from 100 to 400. This domain of concentrations is specific from this type of polymer and can not be generalized, that is why Applicants fine-tuned an induced gelling test in order to determine the accurate concentration of other polymers in order to prolong the release beyond 24 h after administration. The support for this correction can be found in the PCT application WO2005051418.

The Examiner argues that Huille teaches polymer concentrations within the instantly claimed range of a dependent claim. Applicants would like to point out that in Huille, the polymers disclosed are either grafted with a methyl group, an ethyl group or an hydrophobic group derived from dodecanol and thus the "induced gelling" critical concentrations of these polymers are different from the range of concentrations claimed in

claim 19 which is concerned by polymers having an hydrophobic group derived from tocopherol or cholesterol, $1\% \leq [n/(n + m)] \times 100 \leq 10\%$, and n + m varies from 100 to 400. Furthermore as you can see in example 8 and in figure 1, for the concentration range disclosed by Huille, the release of the insulin is not prolonged beyond 24h after administration. The present invention permits to prolong the release of active principle beyond 24h after administration by determining critical concentration through an induced gelling test. The induced gelling test and the critical concentration were not disclosed by Huille. And this critical concentration was not easy to find because an IG test is not a routine test that a person having ordinary skill could or would do without indications. Furthermore, the induced gelling test is not specific to one particular polymer, because the IG test can be done with every polymer which may be used in the formulation.

Applicants would like to note that the result which is reached by the present invention is to prolong the release in vivo and is not restrictive to form a gel. Regarding Akiyoshi, the polymer disclosed is cholesterol-bearing pullulan and not a polyamino acid comprising aspartic units, glutamic units, or both aspartic and glutamic units with hydrophobic groups selected from the group consisting of α-tocopherol, cholesterol and n-dodecanol. Akiyoshi does not teach how to prolong the release beyond 24h after administration. BSA is used in this document to study the dissociation of Insulin from the α-Chy-CHP complex. The release of Insulin is probably caused by exchange between the two proteins due to the slight differences in their binding strength to the CHP self-aggregate. On the contrary, BSA in the present invention is not used to obtain a dissociation of the active principle from the polymer but to determine the critical concentration by which the accurate release is obtained in vivo. Akiyoshi does not teach such a concentration.

The Examiner argues that generally differences in concentration does not support the patentability of the subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical. Applicants respectfully maintain that the IG test, which was not disclosed in the prior art, permit to determine the concentration for which the release is prolonged beyond 24h after administration. In example 7, the formulations E and F have polymer concentrations greater than the gelling concentration C1 whereas the formulation G has a concentration below the concentration C1. As seen in table 5, the formulations E and F, which belong to the selection according to the invention, have a

considerably longer release time than the formulation G, which does not belong to the selection according to the invention. The Tmax for the formulations E and F is about 32 hours contrary to the formulation G for which the Tmax is about 4 hours. These results show that this concentration which has been determined by using the IG test according to the invention is critical for the increase of the release time.

Therefore, Huille does not teach nor suggest how to obtain the accurate concentration for the formulation prolonging the release of the active principle beyond 24 hours after administration. Neither Lambert, nor Singh or Akiyoshi does teach or suggest such a way to obtain this critical concentration. In conclusion, the cited references do not, either singly or in combination, teach or suggest the use of an induced gelling test in order to determine critical concentration to obtain a liquid pharmaceutical formulation prolonging the release of interleukin beyond 24 hours after administration as claimed in claim 3.

For at least these reasons, independent claim 3 is patentable over Huille in view of Lambert, Singh and further in view of Akiyoshi. Dependent claims 5, 7, 9, 10, 12-15, 17-26, and 35-42 depend from independent claim 3 and add further patentable features to the patentable features of the independent claim. Therefore, claims 3, 5, 7, 9, 10, 12-15, 17-26, and 35-42 are patentable over Huille in view of Lambert, Singh and further in view of Akiyoshi. Withdrawal of the rejections and allowance of all claims are respectfully requested.

Obviousness - Type Double Patenting Rejections

The examiner rejects claims 3-7, 9, 10, 12-15, 18-22, 24, and 36-40, alleging they are obvious over claims 1-35 of Huille, as evidenced by the Handbook and Akioyshi. Applicants hereby incorporates the above arguments.

Huille does not teach the relation between an in vitro protein-induced gelling phenomenon, the critical concentration 0.9 C1 and a great increase in the release time of the Interleukin. Akiyoshi does not cure this deficiency. The combination of these references therefore cannot render the instant invention of claim 3 obvious. All other claims alleged by the examiner to depend directly or indirectly from claim 3 and therefore, contain all the

limitations of claim 3, and thus are not obvious. Applicants therefore respectfully request to this rejection be withdrawn.

New Objections/Rejections – Necessitated by Amendment

Claim 3 is objected for informalities. Applicant has amended claim 3 in order to place the claims in proper form, and therefore request the objection be withdrawn.

The Examiner rejects claims 3, 41 and 42 under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. To expedite prosecution Applicants cancelled these claims.

Conclusion

In view of the foregoing amendments and remarks, the Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims. Applicants believe no fee is due with this submission. If a fee is due, however, the U.S. Patent and Trademark Office is authorized to charge any additional fees that may be required in conjunction with this submission to Deposit Account Number 50-2228, referencing matter number 022290.0158PTUS, from which the undersigned is authorized to draw.

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